Realizing Nature's Potential

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Dr. Gordon Cragg

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Bioprospecting in the Cragg Era: Accomplishments and the Road Ahead

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The natural products research community anticipated the basic elements of the Convention on Biological Diversity well before its signing in 1992, recognizing the need to share benefits with both countries and communities based on their contribution of sovereign plant genetic resources and traditional knowledge, both of which are critical elements in drug discovery efforts. The Natural Products Branch of the Developmental Therapeutics Program of the National Cancer Institute (NCI) played an innovative and key role in fostering equitable collaborative relationships in countries where plant material was collected via contracting institutions, in its program to supply raw materials for the discovery of new anticancer, and later, new anti-HIV drugs. These agreements, which came to be known as NCI's Letter of Intent and Letter of Collection, arose from deliberations in the late 1980s and quickly became the standard, not only for NCI's benefit-sharing framework in many countries in which it worked, but also for many academic and commercial agreements as well. In the rich and lengthy dialog that has followed the Convention on Biological Diversity entering into force in 1993, the NCI program serves as a model mechanism for access and benefit-sharing policies, including building scientific capacity in developing countries. The New York Botanical Garden received an NCI collections contract in 1986 to work in the Neotropical region. As part of that project, our group implemented a project in Belize to inventory the biodiversity and traditional uses of plants by local people, which over the years grew into a nationwide effort. Gordon Cragg played a vital role in making these NCI collection projects possible in many areas of the world, and his contributions will be discussed.

Introduction

It was a great pleasure to learn from Jim Miller that the William L. Brown Center of the Missouri Botanical Garden would bestow upon Dr. Gordon Cragg its highest honor, the William L. Brown Award, in recognition of his work in natural products research and the search for novel therapies for human illness. This recognition and symposium in his honor are particularly fitting, as Gordon Cragg has aided so many scientists and students working in the natural products field, as well as influenced the thinking of policy makers and others regarding the importance of biodiversity and genetic preservation. My first interactions with Gordon were through his work at the Natural Products Branch of the Developmental Therapeutics Program (DTP) at the National Cancer Institute (NCI), and over several decades I have come to know him as a friend and colleague.

In 1986, The New York Botanical Garden (NYBG) was awarded a collections contract for the Neotropical region and was charged with collecting higher plant samples for study in the NCI's laboratories. At the inception, the project was focused on identifying compounds with anticancer activity via a series of in vitro screens, with anti-HIV screens added several years later. One of our earliest discussions was at a contractor's meeting at the NCI, in which three groups—from NYBG, the Missouri Botanical Garden, and the University of Illinois at Chicago—received guid-

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[2]I am grateful to my many colleagues at NYBG who contributed to the work described herein, in particular Drs. Douglas Daly and Hans Beck, who were co-PIs on the NCI contract. In addition, thanks are due to the hundreds of local individuals and plant taxonomists who made it possible to collect and identify the specimens sent to the NCI for study. Dr. James Miller was kind enough to invite me to the meeting in St. Louis, and our conversations, for which I am grateful, helped shape my presentation. Finally, I thank Dr. David Newman of the DTP/NCI for providing me with data concerning the project, as well as information on the updated letters in use at present.

ance as to the protocols to be used in making field collections at sites around the world. Each institution was represented by a principal investigator: Dr. Enrique Forero from Missouri, Dr. Doel Soejarto from Illinois, and myself representing NYBG. The three of us had been influenced by the great tropical ethnobotanist, Harvard Professor Richard Evans Schultes, who was, at heart, more Amazonian than Bostonian. His great sense of respect for the indigenous peoples, with whom he spent so many decades, had been passed along to the three of us, as well as to many others he had mentored. We accepted the fact that, without the support, guidance, and participation of the local people that we worked with, our accomplishments would wither. Thus, as the three of us sat around the table with our NCI colleagues, a consensus emerged that we would raise the question of intellectual property and benefit-sharing for the many local people and institutions that would participate in this global search for new therapies.

Up to that point in time, many of those involved in natural products research, as Dr. Norman Farnsworth takes such delight in pointing out, believed that the "tooth fairy" collected and delivered plant samples to their laboratories, ignoring the months and years of relationship building, risky travel and fieldwork, and complicated levels of permits needed to source and deliver plant samples and their associated herbarium vouchers. Given that there were no international treaties governing the collection and transport of plant materials to be evaluated for new therapies at that time, this was not a major part of the protocol being discussed. So, after a few minutes of conversation, Forero, Soejarto, and I decided to make a joint statement to the assembled group of NCI staff. We explained that the political, social, and economic landscape upon which this type of work was undertaken had been changing, and local people, along with their communities and governments, were questioning whether or not any benefits would be provided to their countries and villages as a result of their participation in this hunt for new pharmaceuticals. Providing firsthand reports from the field, we spoke of being compared to those historic figures who would extract resources from faraway places and take them for the benefit of the developed world, where people could afford the cost of anticancer therapies. And we noted how the ethical position of the United States, as the funder of this research, could be undermined by extractive projects such as these, said to be for the public good. I recall the reaction of the larger group as a sort of disbelief at first, not understanding why a group of mere contractors, and field botanists at that, could bring up this issue, when the program was already in place. A somewhat tense discussion followed, and it became clear to the three of us that we were on very thin ice. However, one voice cut through the tension, that of Gordon Cragg. He acknowledged that it might very well be a good idea to rethink the NCI's position on benefit-sharing, and by addressing this embryonic but controversial topic, and indeed leading the way rather than avoiding it, the U.S. and NCI could accomplish a great deal more for the field and, ultimately, the project.

What followed in the many years since that first meeting was an extraordinary effort by Gordon and his colleagues—from many sectors—to craft a benefit-sharing document that would be widely accepted by the diverse parties involved in the NCI's international natural products programs. This was accomplished, with the first version followed by dozens of revisions suited to the particular country a team was working in, as Gordon and the NCI staff circulated drafts to collectors, scientists, policy makers, governmental officials, indigenous peoples, and even critics.

The first documents that resulted from these deliberations were known as the NCI Letter of Intent (LOI) and, in a later version, the NCI Letter of Collection (LOC). These letters were comprehensive, and espoused fairness,

honesty, and transparency in all work that was to be accomplished under the aegis of the DTP. The agreements quickly became the standard not only for NCI's benefit-sharing framework in the dozens of countries in which it worked, but also for many academic and commercial agreements as well. The LOC was executed between an organization in the country where the plants were collected and the DTP of the NCI. The most current letter is presented as Appendix 1 of this paper. In the rich and lengthy dialog that proceeded and has followed the Convention on Biological Diversity (CBD) entering into force in 1993, the NCI program serves as a model mechanism for access and benefit-sharing policies, including building scientific capacity in developing countries. At its inception, the CBD had three main goals: the conservation of biological diversity; the sustainable use of its components; and the fair and equitable sharing of benefits derived from this use. These three themes were spelled out in 42 articles, including Article 8J, which discussed traditional knowledge, innovations, and practices, along with the need for mechanisms for indigenous peoples to share in the benefits arising from the discovery and commercialization of biodiversity. It was no coincidence that the major thrust of the United Nation's CBD paralleled that of the National Cancer Institute DTP's LOI. And I don't think it hyperbole to credit a humble individual who knew that he could accomplish anything in government, as long as it did not matter who received the credit for doing so, with influencing—rather, defining—the shape of the CBD. In the mid-1990s, an updated version of the LOI that acknowledged local capacity in natural products research was developed and used as a deliberate component of the process to source collections and strengthen that capacity.

Despite the fact that the United States was not a signatory to the CBD, there was great interest in the botanical community to move forward with an international agreement that governed our own research, plant collection, and plant exchange programs around the world. Following five years of international workshops involving many dozens of colleagues from botanical gardens, universities, and museums (both large and small), a document entitled *Principles on Access to Genetic Resources and Benefit-sharing for Participating Institutions* was produced in December 2000. This document pledged to "honor the spirit and letter of the Convention on Biological Diversity and laws related to access to genetic resources and associated traditional knowledge and benefit-sharing" with regard to: acquisition of genetic resources; curation, use, and supply of genetic resources; and benefit-sharing, pledging to: prepare a policy to ensure this would be implemented as part of the institutional structure and employ written agreements that were transparent, fair, and constituted best practice. A set of *Explanatory Texts,* comprising 101 pages of sample agreements, definitions, and templates accompany the Principles (http://www.kew.org/conservation/agrbs-policy.pdf). These principles were intended to facilitate the kind of plant collection and research intended by the CBD, and once again, were heavily influenced by the NCI's LOI and LOC. To date, 22 institutions have signed on to the Principles, helping to guide their important international field programs.

I—along with NYBG colleagues Drs. Douglas Daly and Hans Beck, NYBG's principal investigators on these contracts—worked in several of the 18 field sites where our contracts operated from 1986–1996. My personal focus was on Central America and, in particular, Belize. In total we at the NYBG collected 16,276 bulk samples of higher plants for the DTP from 1986–1996, comprising 218 plant families (77% of the families present in the Neotropical region), 1,421 genera (33% of the genera present in the region), and 2,504 species (ca. 3% of the total number described from the region). In Belize, our active collaboration with Drs. Rosita Arvigo and Gregory Shropshire, as well as the

Traditional Healer's Foundation of Belize and many other governmental and non-governmental organizations, resulted in the collection of 2,392 extracts from multiple plant parts, comprising 108 of the 209 plant families, 388 of the 1,219 genera, and 529 of the 3,408 species present in that nation.

FIELDWORK IN BELIZE: THE BELIZE ETHNOBOTANY PROJECT

Belize is a Central American country located on the Caribbean coast, south of Mexico and east of Guatemala. It has a population of 250,000 inhabitants spread over 8,867 square miles, giving a low population density of 28 persons per square mile. Over 70% of the country is under natural forest, and protected areas now cover 36% of the landmass. Despite the small size of the country, its ecosystems are varied and its ethnicity diverse, giving rise to a rich culture with respect to traditional healing. The ethnic diversity ranges from groups of indigenous Maya and the Black Caribs (Garinagu), through the Creole descendants of African slaves, to the more recent Central American and Asian immigrants. Among some of these ethnic groups (especially the Maya and the Garinagu), the use of medicinal plants is spiritual and is linked to myths, rituals, and religion. The knowledge acquired by healers has long ancestral origins.

It was against this backdrop that the Belize Ethnobotany Project was launched in 1988, initially through funding received for plant collecting from the NCI/DTP. The project was a collaborative endeavor involving the Ix Chel Tropical Research Foundation, Belize Center for Environmental Studies, Faculty of Agriculture and Natural Resources of the University of Belize, Agriculture Research and Development Station in Central Farm, The Belize Zoo and Tropical Education Center, Belize Forestry Department, Belize Association of Traditional Healers, Traditional Healers Foundation of Belize, and NYBG.

The most significant goal of the project was to conduct an inventory of the floristic and ethnobotanical diversity of Belize, a country with large tracts of intact forest. The project carried out over 100 collection trips to various locales, and collected over 8,000 plant specimens by the end of 2000. We gathered traditional knowledge provided by dozens of traditional healers and bushmasters of Mopan, Yucateco, and Kekchi Maya, Ladino, Garinagu, Creole, East Indian, and Mennonite descent. Another significant objective was to help foster the teaching and use of traditional knowledge as it relates to plants and the environment. Additionally, the project aimed at promoting conservation of knowledge and biodiversity, through various local initiatives including displays, seminars, post-secondary classes, youth camps, school competition, field trips, and guest lectures. A major output of these local initiatives was the establishment of the first ethnobiomedical forest reserve in the world, dedicated to the conservation of medicinal plants. A more complete discussion of this multifaceted project is presented in Balick and O'Brien (2004).

A program involving short-term, medium-term, and long-term benefits to participants was implemented as part of this project. An example of short-term benefits was the provision of resources to the individuals and the communities in which they lived. Medium-term benefits included formation of the Belize Association of Traditional Healers and later the Traditional Healer's Foundation, which provided royalty payments from the sale of a book on the useful plants of Belize entitled *Rainforest Remedies: One Hundred Healing Herbs of Belize* (Arvigo and Balick, 1993). Over nearly two decades $26,000 (BZ $52,000) was provided directly through biannual payments to the individuals involved in providing information for this book. Details on how the payments helped these individuals to achieve their own goals are provided in Johnston (1998). Today, *Rainforest Remedies* and an-

Figure 1. Gordon Cragg traveling via horseback in a remote area of the Cayo District, Belize, as part of a site visit.

other book published by the project, *Checklist of the Vascular Plants of Belize: With Common Names and Uses* (Balick, Nee, and Atha, 2000), are important documents in support of conservation and ecotourism in the region, as they are rich with information and lore about Belize and its natural resources. In the longer term, the NCI's documents and policies include payments to be made if any of the plants collected under the project achieve commercial status.

Gordon Cragg and our Contracts Officer Elsa Carlton (Figures 1 and 2) had the opportunity to visit the Belize field site in June 1988, and see firsthand some of the results of their work running the NCI plant collections program. During this visit, we gave the most senior of our local healer/collaborators, Don Elijio Panti, a certificate signed by Gordon, expressing thanks for the former's extraordinary collaboration in this project. To Don Elijio the presentation of this document was a milestone in his long life; recognition by a prestigious outside institution that his work had meaning far beyond the boundaries of his small village of San Ignacio. This document, an example of a non-monetary benefit provided by the project, occupied a place of honor in Don Elijio's humble dwelling for the rest of his life, and when patients came to visit, he proudly explained how he was working with NCI on

Figure 2. Elsa Carlton learning by doing—collecting plant samples in the Cayo District, Belize.

an important study. While this might seem a small detail in the history of this important federal organization, Gordon's enthusiasm for providing this type of respect for a local collaborator was a hallmark of the way in which he led the collections program. So it is quite fitting that we return the favor at the William L. Brown Symposium and honor Gordon in the company of so many of his friends.

CONCLUSION

The title of this paper refers to the "Cragg Era" as it relates to biodiversity and natural products research. Prior to that era, there were few rules of conduct for collectors and investigators, and one encountered often limited and confusing systems of permits and protocols in place in source countries, including the United States. Making collections was, in some ways, a sort of a scientific free-for-all, with the game plan often made up on the spot and most usually influenced in some way by the need for efficiency and speed. However, the attitude of governments and their citizens around the world was changing at the time, and in some places biodiversity-related xenophobia had already set in, prohibiting any collection activity, even at times by local people themselves. Lacking a series of international agreements shaped through discussion and consensus building, the search for new therapies from plants could have come to a halt in many areas of the world. At the risk of sounding trite, I, along with many of my colleagues, believe that Gordon Cragg and his co-workers at the NCI set a new standard for natural products research, both in the laboratory and the field. His willingness to consider local partners as equals, and the many years he spent visiting field sites and making people feel appreciated for their collaboration with the NCI will ensure that this type of research can be continued in many critical locales. At a time when the parameters by which we carry out field-based natural products research are changing on an almost weekly basis (through the establishment of new laws and best practices), trust and relationships have become basic requirements for this work. The post-Cragg era will not be an easy one, as the goal of ensuring equity in our partnerships and conserving biodiversity worldwide has not yet been achieved. We who continue to seek an understanding of the diversity, wisdom, and potential of nature owe a great debt of gratitude to Gordon Cragg for his untiring contributions to making this quest possible.

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APPENDIX 1

LETTER OF COLLECTION
Agreement Between
[Source Country Organization, SCO]
and the
Developmental Therapeutics Program
Division of Cancer Treatment and Diagnosis
National Cancer Institute*

The Developmental Therapeutics Program (DTP), Division of Cancer Treatment and Diagnosis ("DCTD"),

*From the National Cancer Institute web site. Available at: http://ttc.nci.nih.gov/forms/loc.doc.

National Cancer Institute (NCI) is currently investigating plants, micro-organisms, and marine macro-organisms as potential sources of novel anticancer drugs. The DTP is the drug discovery program of the NCI which is an Institute of the National Institutes of Health (NIH), an arm of the Department of Health and Human Services (DHHS) of the United States Government. While investigating the potential of natural products in drug discovery and development, NCI wishes to promote the conservation and sustainable utility of biological diversity, and recognizes the need to compensate [Source Country, SC] organizations and peoples in the event of commercialization of a drug developed from an organism collected within their country's borders.

As part of the drug discovery program, DTP has contracts with various organizations for the collection of plants, micro-organisms and marine macro-organisms worldwide. DTP has an interest in investigating plants, micro-organisms and marine macro-organisms from [Source Country], and wishes to collaborate with the [Source Country Government (SCG) or Source Country Organization(s) (SCO)] as appropriate in this investigation. The collection of plants, micro-organisms and marine macro-organisms will be within the framework of the collection contract between the NCI and the NCI Contractor [Contractor] which will collaborate with the appropriate agency in the [SCG or SCO]. The NCI will make sincere efforts to transfer knowledge, expertise, and technology related to drug discovery and development to the [appropriate Source Country Organization (SCO)] in [Source Country] as the agent appointed by the [SCG or SCO], subject to the provision of mutually acceptable guarantees for the protection of intellectual property associated with any patented technology. The [SCG or SCO], in turn, desires to collaborate closely with the DTP/NCI in pursuit of the investigation of its plants, micro-organisms and marine macro-organisms, subject to the conditions and stipulations of this agreement.

A. The role of DTP, DCTD, NCI in the collaboration will include the following:

1) DTP/NCI will screen the extracts of all plants, micro-organisms and marine macro-organisms provided from [Source Country] for anticancer activity, and will provide the test results to [SCO] on an annual basis. Such results will be channeled via Contractor.
2) The parties will keep the test results and subsequently-developed data confidential until approved for publication by the parties. Before either party submits a paper or abstract containing test results for publication, the other party shall have 60 days to review and, as necessary file a sole or joint patent application in accordance with Article 6.
3) Any extracts exhibiting significant activity will be further studied by bioassay-guided fractionation in order to isolate the pure compounds(s) responsible for the observed activity. Since the relevant bioassays are only available at DTP/NCI, such fractionation will be carried out in DTP/NCI laboratories. A suitably qualified scientist designated by [SCO] may participate in this process subject to the terms stated in Article 4. In addition, in the course of the contract period, DTP/NCI will assist the [SCO], thereby assisting the [Source Country], to develop the capacity to undertake drug discovery and development, including capabilities for the screening and isolation of active compounds from plants, micro-organisms and marine organisms.
4) Subject to the provision that suitable laboratory space and other necessary resources are available, DTP/NCI agrees to invite a senior technician or scientist designated by [SCO] to work in the laboratories of DTP/NCI or, if the parties agree, in laboratories using technology which would be useful in furthering work under this agreement. The duration of such visits would not exceed one year except by prior agreement between [SCO] and DTP/NCI. The designated visiting scientist(s) will be subject to provisions usually governing Guest Researchers at NIH. Salary and other conditions of exchange will be negotiated in good faith. Costs and other conditions of visits will also be negotiated in good faith prior to the arrival of the visiting scientist(s).
5) In the event of the isolation of a promising agent from a plant, micro-organism or marine macro-organism collected in [Source Country], further development of the agent will be undertaken by DTP/NCI in collaboration with [SCO]. Once an active agent is approved by the DTP/NCI for preclinical development, [SCO] and the DTP/NCI will discuss participation by SCO scientists in the development of the specific agent.

The DTP/NCI will make a sincere effort to transfer any knowledge, expertise, and technology developed during such collaboration in the

discovery and development process to [SCO], subject to the provision of mutually acceptable guarantees for the protection of intellectual property associated with any patented technology.

6) DTP/NCI/NIH will, as appropriate, seek patent protection on all inventions developed under this agreement by DTP/NCI employees alone or by DTP/NCI and [SCG or SCO] employees jointly, and will seek appropriate protection abroad, including in [Source Country], if appropriate. All resulting patent applications and patents shall be assigned to the U.S. Department of Health and Human Services and managed by NIH. Under current NIH policy, all inventors of such assigned patents may receive royalties in accordance with said NIH policy for any royalty-bearing license(s) for these patent(s).
7) All licenses granted on any patents resulting from this collaboration shall contain a clause referring to this agreement and shall indicate that the licensee has been apprised of this agreement.
8) Should an agent derived from an organism collected under the terms of this agreement eventually be licensed to a pharmaceutical company for production and marketing, DTP/NCI will request that NIH/OTT require the successful licensee to negotiate and enter into agreement(s) with the appropriate [SCG] agency(ies) or [SCO] within twelve (12) months from the execution of said license. This agreement(s) will address the concern on the part of the [SCG or SCO] that pertinent agencies, institutions and/or persons receive royalties and other forms of compensation, as appropriate.
9) The terms of Article 8 shall apply equally to inventions directed to a direct isolate from a natural product material, a product structurally based upon an isolate from the natural product material, a synthetic material for which the natural product material provided a key development lead, or a method of synthesis or use of any aforementioned isolate, product or material; though the percentage of royalties negotiated as payment might vary depending upon the relationship of the marketed drug to the originally isolated product. It is understood that the eventual development of a drug to the stage of marketing is a long term process which may require 10-15 years.
10) In obtaining licensees, the DTP/NCI/NIH will require the license applicant to seek as its first source of supply the natural products from [Source Country]. If no appropriate licensee is found that will use natural products available from [Source Country], or if the [SCG] or [SCO] as appropriate, or its suppliers cannot provide adequate amounts of raw materials at a mutually agreeable fair price, the licensee will be required to pay to the [SCG] or [SCO] as appropriate, compensation (to be negotiated) to be used for expenses associated with cultivation of medicinal organisms that are endangered or for other appropriate conservation measures. These terms will also apply in the event that the licensee begins to market a synthetic material for which a material from [Source Country] provided a key development lead.
11) Article 10 shall not apply to organisms which are freely available from different countries (i.e., common weeds, agricultural crops, ornamental plants, fouling organisms) unless information indicating a particular use of the organism (e.g., medicinal, pesticidal) was provided by local residents to guide the collection of such an organism from [Source Country], or unless other justification acceptable to both the [SCG or SCO] and the DTP/NCI is provided. In the case where an organism is freely available from different countries, but a phenotype producing an active agent is found only in [Source Country], Article 10 shall apply.
12) DTP/NCI will test any pure compounds independently submitted by the [SCG or SCO] scientists for antitumor activity, provided such compounds have not been tested previously in the DTP/NCI screens. If significant antitumor activity is detected, further development of the compound may, as appropriate, be undertaken by DTP/NCI in consultation with the [SCG or SCO].

    Should an NCI/NIH patent on an agent derived from the submitted compound(s) eventually be licensed to a pharmaceutical company for production and marketing, DTP/NCI will request that NIH/OTT require the successful licensee to negotiate and enter into agreement(s) with the appropriate [SCG agency(ies) or SCO] within twelve (12) months from the execution of said license. This agreement will address the concern on the part of the [SCG or SCO] that pertinent agencies, institutions and/or persons receive royalties and other forms of compensation, as appropriate.
13) DTP/NCI may send selected samples to other organizations for investigation of their anti-cancer, anti-HIV or other therapeutic potential. Such samples will be restricted to those collected by NCI

contractors unless specifically authorized by the [SCG or SCO]. Any organization receiving samples must agree to compensate the [SCG or SCO] and individuals, as appropriate, in the same fashion as described in Articles 8-10 above, notwithstanding anything to the contrary in Article 11.

B. The role of the Source Country Government ("SCG") or Source Country Organization(s) ("SCO") in the collaboration will include the following:

1) The appropriate agency in [SCG or SCO] will collaborate with Contractor in the collection of plants, micro-organisms and marine macro-organisms, and will work with Contractor to arrange the necessary permits to ensure the timely collection and export of materials to DTP/NCI.
2) Should the appropriate agency in [SCG or SCO] have any knowledge of the medicinal use of any plants, micro-organisms and marine macro-organisms by the local population or traditional healers, this information will be used to guide the collection of plants, micro-organisms or marine macro-organisms on a priority basis where possible. Details of the methods of administration (e.g., hot infusion, etc.) used by the traditional healers will be provided where applicable to enable suitable extracts to be made. All such information will be kept confidential by DTP/NCI until both parties agree to publication.

   The permission of the traditional healer or community will be sought before publication of their information, and proper acknowledgment will be made of their contribution.
3) The appropriate agency in [SCG or SCO] and Contractor will collaborate in the provision of further quantities of active raw material if required for development studies.
4) In the event of large amounts of raw material being required for production, the appropriate agency of the [SCG or SCO] and Contractor will investigate the mass propagation of the material in [Source Country]. Consideration should also be given to sustainable harvest of the material while conserving the biological diversity of the region, and involvement of the local population in the planning and implementation stages.
5) [SCG or SCG] and SCO scientists and their collaborators may screen additional samples of the same raw materials for other biological activities and develop them for such purposes independently of this agreement.

This agreement shall be valid as of the date of the final authorized signature below for an initial period of five (5) years, after which it can be renewed by mutual agreement. It may be amended at any time subject to the written agreement of both parties. Copies of such amendments will be kept on file at both of the addresses indicated below.

For the National Cancer Institute:

_____

John E. Niederhuber, M.D.
Director, National Cancer Institute

_____

Date

Mailing and contact address:
Technology Transfer Branch
National Cancer Institute at Frederick
Fairview Center, Suite 500
1003 - W. 7th Street
Frederick, Maryland 21701-8512 U.S.A.
Telephone: 301-846-5465
Facsimile: 301-846-6820

For [SCI] or [SCO]:

_____

Name (typed):
Title:

_____

Date

mailing and contact address:

_____

_____

_____

_____